REMARKS

Upon entry of the present Amendment, claims 85 and 91-100 will be pending. Claims 86-90 are cancelled as non-elected claims. Applicant reserves the rights to pursue the canceled subject matter in a subsequent application. The amended claim 85 and new claims 91-100 find support throughout the specification and claims as originally filed. The above-described amendments do not introduce any new matter into the present application.

Due date for responding to the present Office Action

The present Office Action was mailed out on October 12, 2002. An one-month, instead a three-month, due date was indicated in the Office Action. However, in a teleconference between the Examiner and the undersigned on November 6, 2002, the Examiner indicated that the one-month due date was an error and a response to the present Office Action is due three months from its mailing date, *i.e.*, January 11, 2003. Accordingly, applicant respectfully requests that this one-month to three-month due-date change be clearly indicated in the record of the present application.

Restriction requirement

Applicant appreciates the Examiner's acknowledgement of Applicant's election of Group I, claim 85. Claims 86-90 are cancelled as non-elected claims.

Rejections under 35 U.S.C. § 112

Written description

Claim 85 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. It is alleged that there is insufficient written description to show that Applicant was in possession of a bridge molecule, other than a bispecific monoclonal antibody.

This rejection is overcome by the replacement of "bridge molecule" with a "bispecific monoclonal antibody" in claim 85.

Enablement

Applicant appreciates the Examiner's recognition that the present specification provides an enabling disclosure for a method of preparing an immunogenic composition, comprising the steps of: providing an autologous tumor cell, incubating said cell in IPNγ and TNFα providing a CD28:gp115 or CD28:gp55 bispecific monoclonal antibody bridge molecule, attaching the bridge molecule to the tumor cell, and collecting a pharmaceutically effective amount of the target diseased cell with the attached bridge molecule.

Accordingly, new claim 100 is enabled.

The Examiner, nevertheless, rejected claim 85 under 3S U.S.C. 112, first paragraph for alleged non-enablement. First, regarding the breadth of the claims, it is alleged that the specification defines a target diseased cell as any cell causing, propagating, aggravating, or contributing to a disease in a patient mammal. It is also alleged that the definition encompasses not only tumor and pathogen infected cells, but completely normal cells under many conditions.

This ground for rejection is overcome by the replacement of "target diseased cell" with "target tumor or pathogen infected cell" in claim 85.

Second, regarding part (c) of claim 85, the Examiner made the following statements:

> Further regarding the breadth of the claims, part (c) claim recites that the bridge molecule need bind only "one or more costimulatory molecules on a surface of one or more T cells" (presumably to provide a required costimulatory activation signal). The specification discloses that a "costimulatory molecule can be essentially *any* CD marker from CDla to CDW130.
>
> First, it must be noted that many of the disclosed markers are never expressed by T cells, for example CD19 (a B cell marker) and CDS3 (a dendritic cell marker). Thus, a method that includes a binding step that could not happen must be considered highly unpredictable. Second, even certain markers that are expressed on T cells, such as CD4 or CD8, play no part in costimulation, indeed the activation of markers such as CD4 or CD8 alone is well-known in the art to induce T cell anergy, *i.e.,* the opposite effect from stimulation (see for example, January *et. al.*, 1994).

Apparently, the Examiner relied upon the disclosure at page 7, line 27 through page 8, line 15 of the present specification for making this rejection. However, it is respectfully submitted that the Examiner's reliance on this passage is misplaced. This passage lists CD1-130, as well as other factors, as costimulatory molecules for any effector cells, not just T cells. Claim 85, on the other hand, is limited to the use of a costimulatory molecule for T cells. Accordingly,

the fact that several factors listed in the passage are not costimulatory molecules for T cells does not show that claim 85 is not enabled.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). A sufficient disclosure must exist as of the application filing date. *White Consolidated Indus., Inc., v. Vega Servo-Control, Inc.*, 218 USPQ 961 (Fed. Cir. 1983). However, a patent need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent, Inc.*, 3 USPQ2d 1737 (Fed. Cir. 1987). Since claim 85 is limited to the use of a costimulatory molecule for T cells and since what constitutes a costimulatory molecule for T cells is well known in the art (as evidenced by the reference cited by the Examiner), there is no undue burden on the skilled artisans to choose a particular costimulatory molecule for T cells to be used in the method of claim 85. Accordingly, this ground for rejection is respectfully traversed.

Third, regarding the working examples of the specification, it is alleged that at least one of the target diseased cells absolutely requires cytokine induction to be immunogenic (specification page 23). It is also alleged that cytokine induction is not a recited method step of the instant claims.

This ground for rejection is overcome by the addition of a cytokine treatment step in claim 85.

It is respectfully submitted that the rejection of claim 85 under 35 U.S.C. § 112 is overcome by the above remarks and/or amendments and must be withdrawn.

Rejection under 35 U.S.C. § 102

Claim 85 is rejected under 35 U.S.C. 102 (b) as allegedly being anticipated by Shi *et al.* (1996, previously of record). Shi *et al.* is alleged to teach a method of preparing an immunogenic composition, comprising the steps of: providing an autologous target diseased cell (human liver cancer cells), increasing concentration of primary T cell activation molecules or costimulatory T cell activation molecules in the target diseased cell (treatment with cytokines), providing a bridge molecule including one or more binding sites for one or more costimulatory molecules on a surface of one or more T cells of a patient mammal (a CP28:gp115 bispecific antibody), attaching the bridge molecule to the target diseased cell, and collecting a

pharmaceutically effective amount of the target diseased cell with the attached bridge molecule. The Examiner noted that, in the reference, the diseased cells were used to activate TILs or PBLs *in vitro*. However, the Examiner alleged that it would have been an inherent property of said activation that the -diseased cells would have been collected before said *in vitro* activation. The Examiner alleged that Shi *et al.* clearly anticipates the claimed invention.

The present application is a CIP of Serial No. 08/875,527, filed June 11, 1997, which claims priority of a provisional application Serial No. 60/019,639, filed June 12, 1996. Accordingly, the effective U.S. filing date of the present application for 35 U.S.C. § 102(b) analysis is June 12, 1996. MPEP 706.02 and 2133. Since Shi *et al.* was published in March or April. 1996, Shi *et al.* is not a 102(b) prior art. Instead, Shi *et al.* is a 102(a) prior art. In view of the Declaration of Yajun Guo pursuant to 37 C.F.R. § 1.132, the rejection of claim 85 based on Shi *et al.* has been overcome. MPEP 2132.01.

It is respectfully submitted that the rejection of claim 85 under 35 U.S.C. § 102 is overcome by the above remarks and/or amendments and must be withdrawn.

CONCLUSION

Applicant respectfully submits that the rejections of claim 85 under 35 U.S.C. §112, first paragraph and the rejection under 35 U.S.C. 102 have been overcome by the above remarks and/or amendments. Early allowance of the pending claims 85 and 91-100 are earnestly requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this

document to **Deposit Account No. 03-1952** referencing **532732000220**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: Jan. 13, 2003

Respectfully submitted,

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